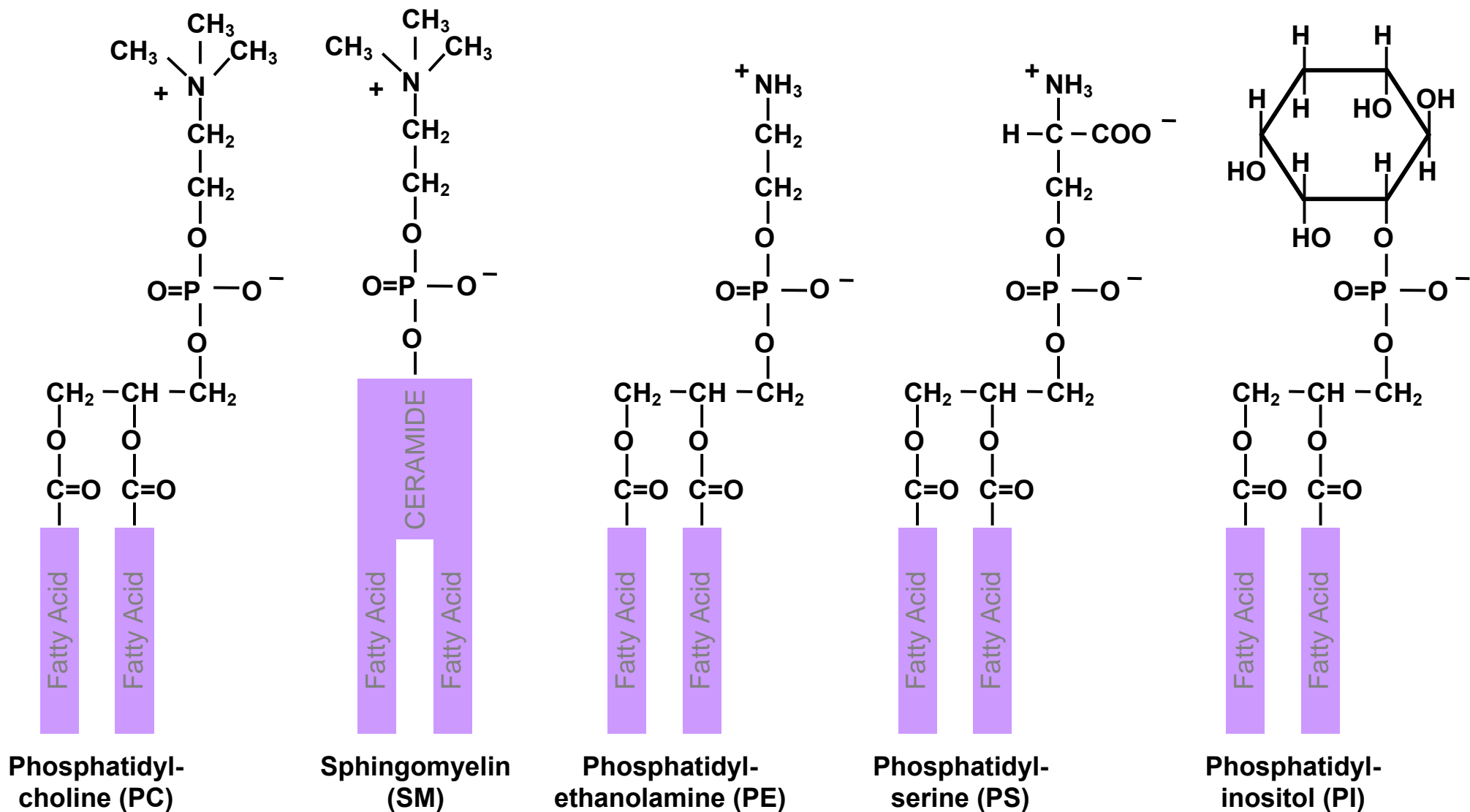


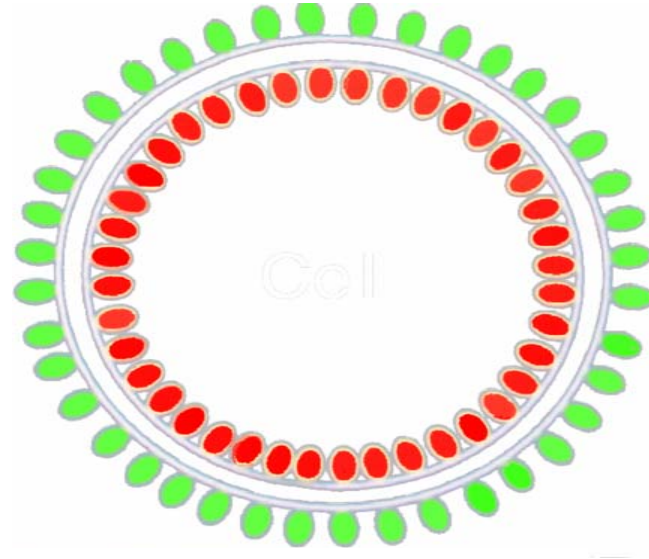
TARVACIN™ ANTIVIRAL

**A NOVEL MONOCLONAL ANTIBODY BASED
THERAPY FOR ENVELOPED VIRUSES**

MAJOR PHOSPHOLIPIDS OF THE PLASMA MEMBRANE



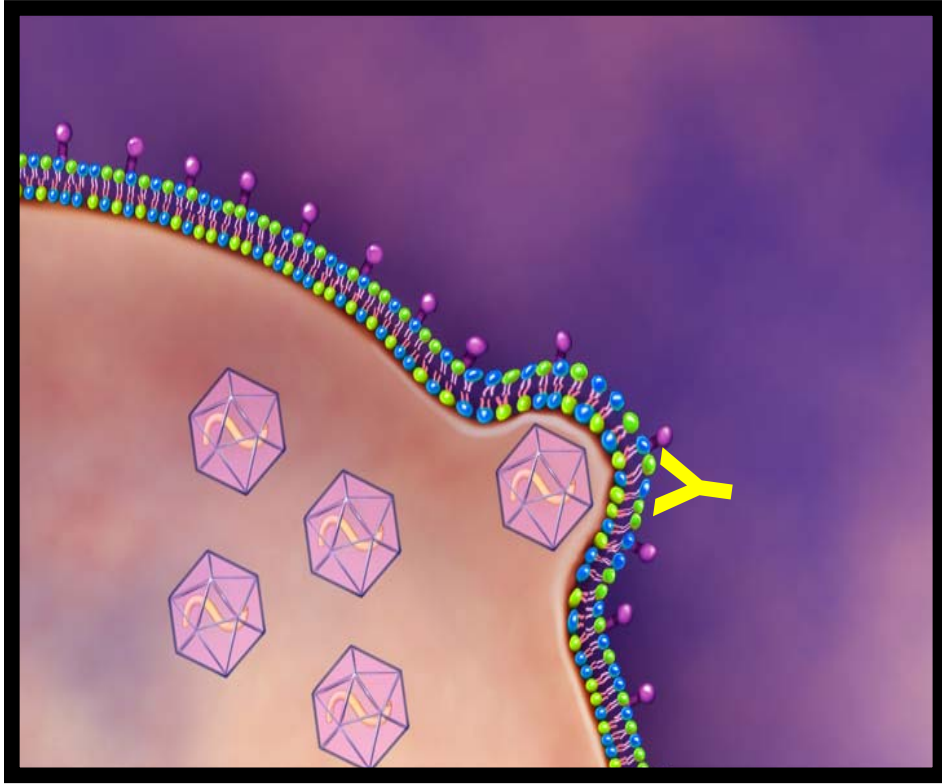
AMINOPHOSPHOLIPIDS (PS and PE) ARE LARGELY ABSENT FROM THE SURFACE OF RESTING MAMMALIAN CELLS



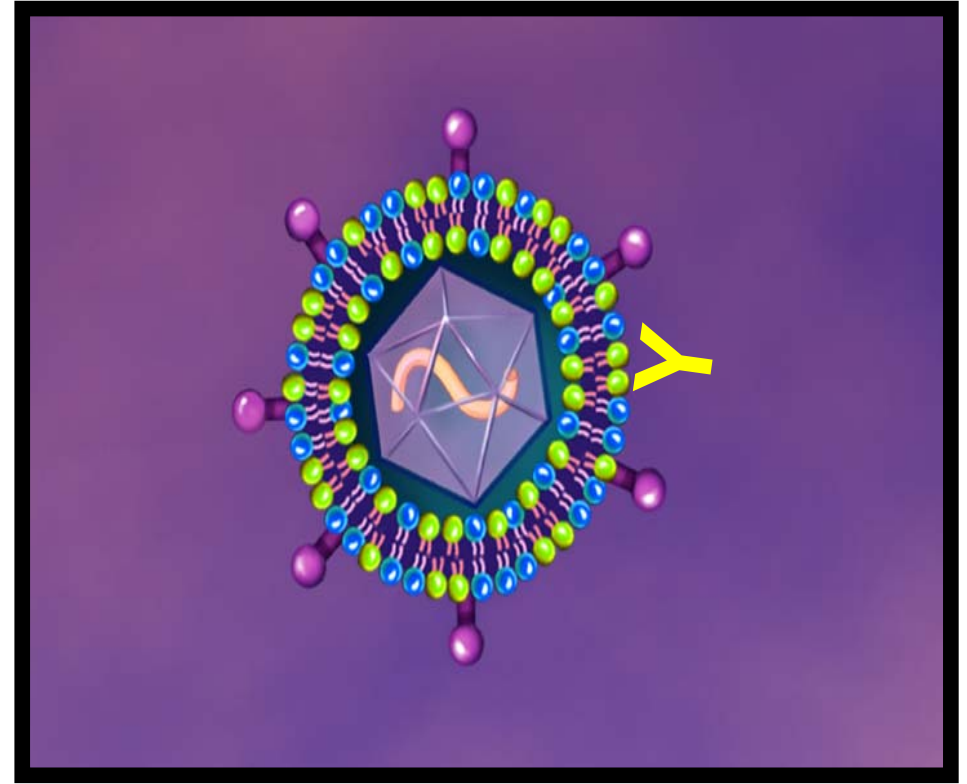
● = aminophospholipids (PS and PE)

● = choline-containing phospholipids (PC, SM)

TARGETING EXTERNAL PS



VIRUS-INFECTED CELL



ENVELOPED VIRUS

OUR WORKING HYPOTHESIS

The exposure of anionic phospholipids on the surface of virus-infected cells and virus envelopes is a general phenomenon

Exposed anionic phospholipids serve as targets for the treatment of virus infections

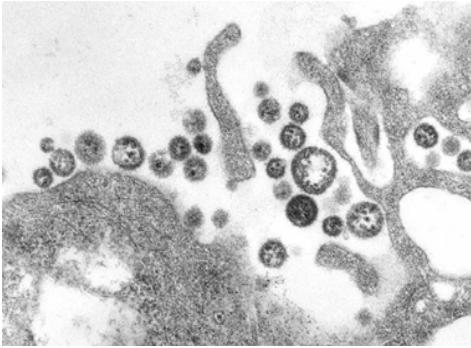


SPECIFICITY OF MONOCLONAL ANTIBODIES

Name	Isotype	Specificity	Serum cofactor
3G4	Mouse IgG ₃	PS	β ₂ -glycoprotein 1
Tarvacin	Human-mouse chimeric	PS	β ₂ -glycoprotein 1

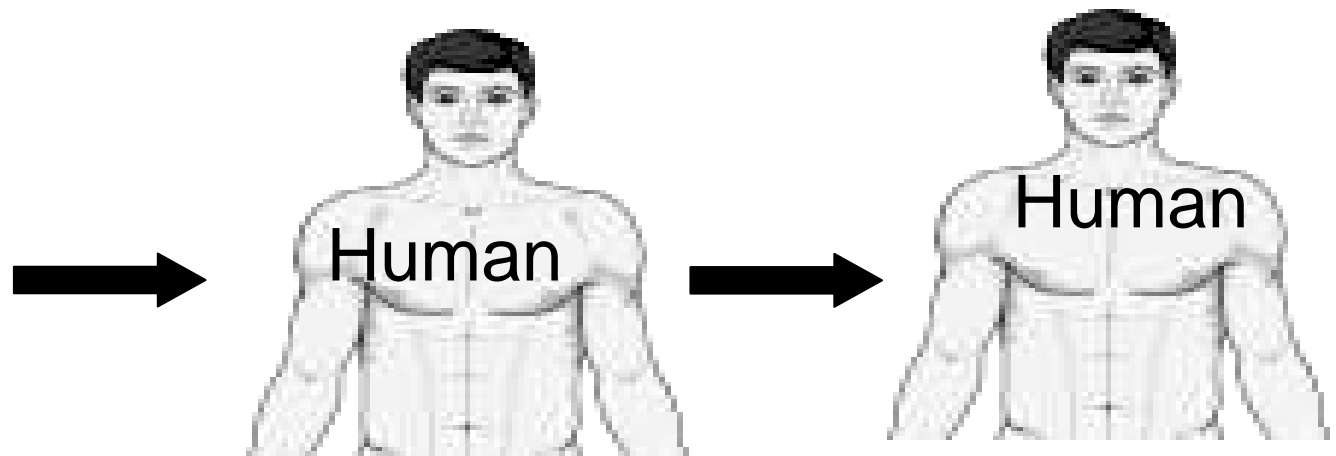
APPLICATION FOR BIODEFENSE

LASSA FEVER VIRUS

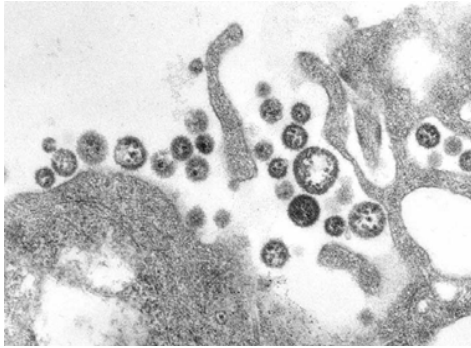


Lassa fever virus is on the CDC Category A list of potential bioterrorism agents

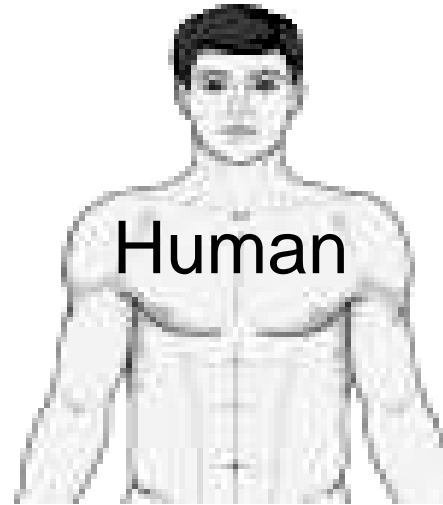
Causes ~3000 deaths annually



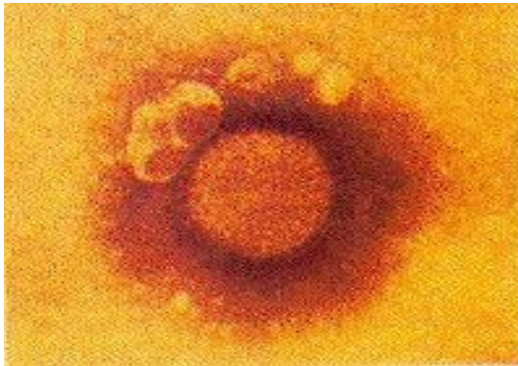
MODELS OF DISEASE



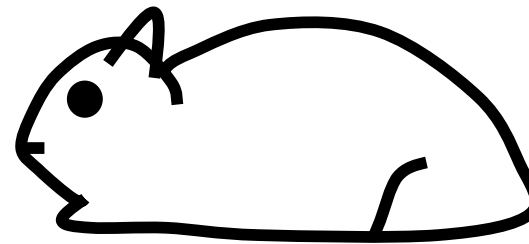
Lassa Virus



- Virus in tissue
- Fever
- Hemorrhage



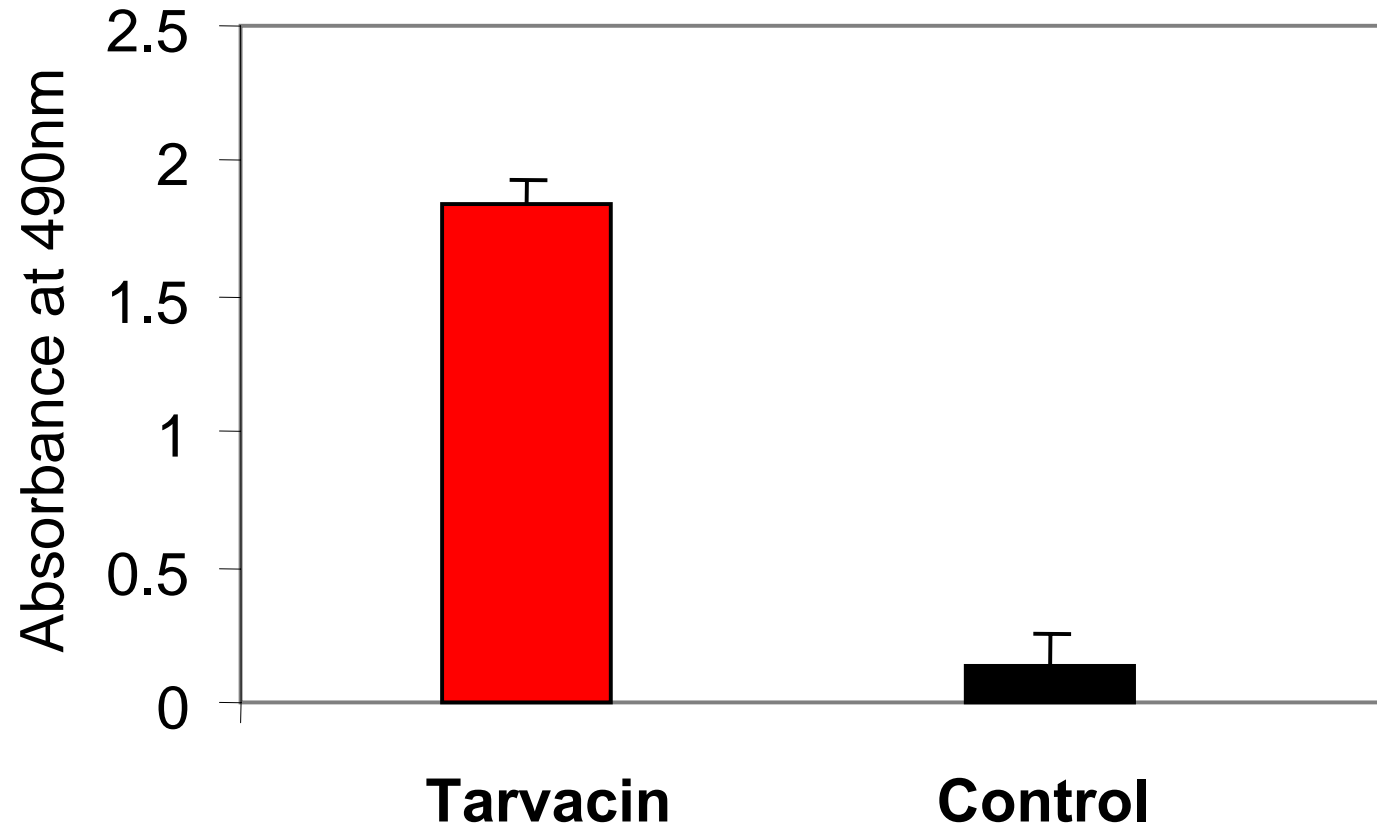
Pichinde Virus



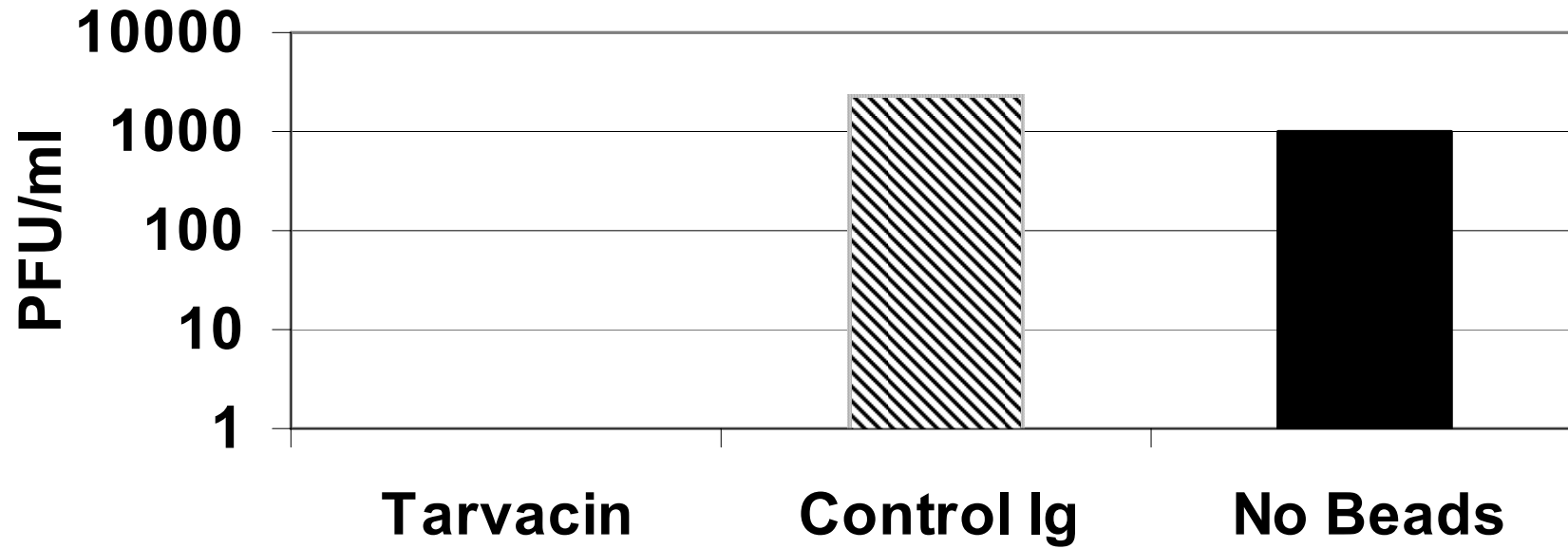
guinea pig

- Virus in tissue
- Fever
- Hemorrhage

BINDING OF TARVACIN TO PICHINDE VIRUS

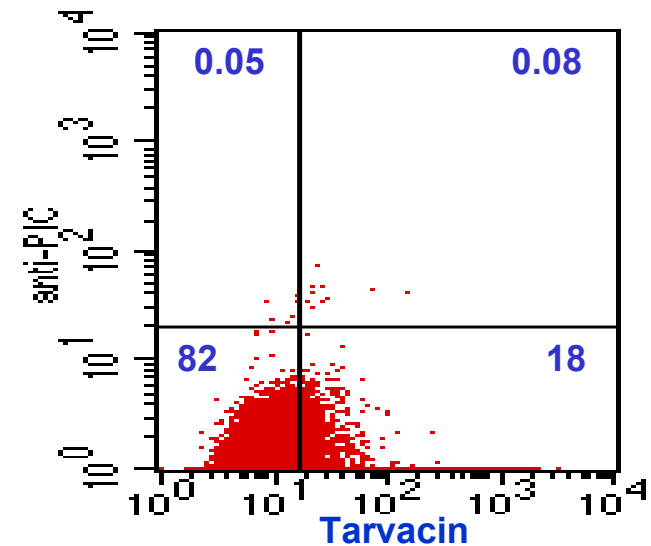
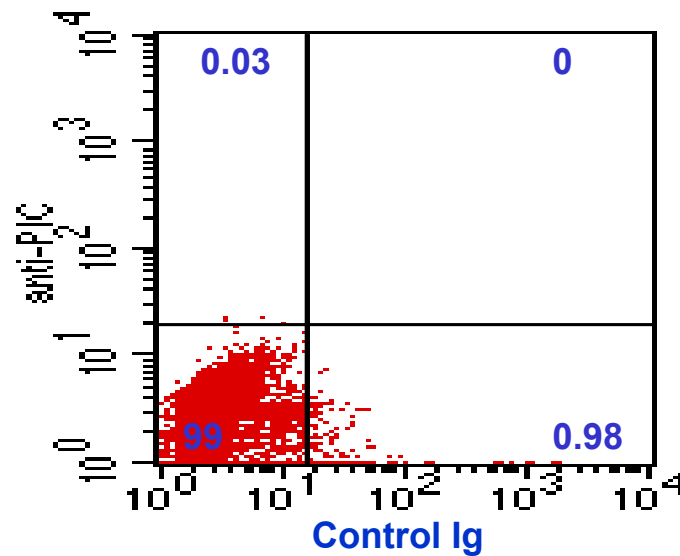


TARVACIN BINDS TO INFECTIOUS PICHINDE VIRUS

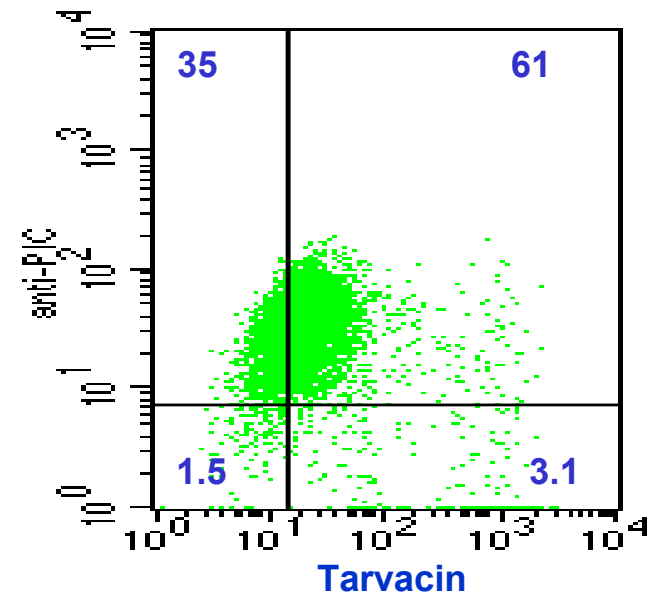
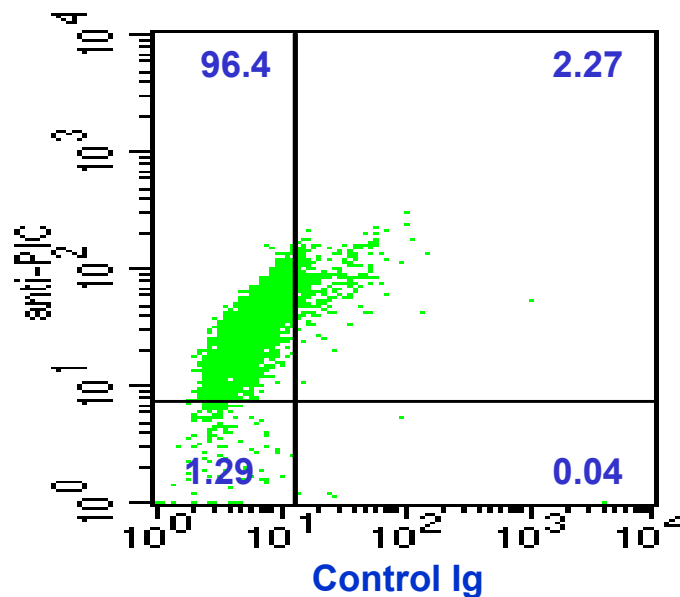


BINDING OF TARVACIN TO P388D1 CELLS INFECTED WITH PICHINDE VIRUS

No Virus

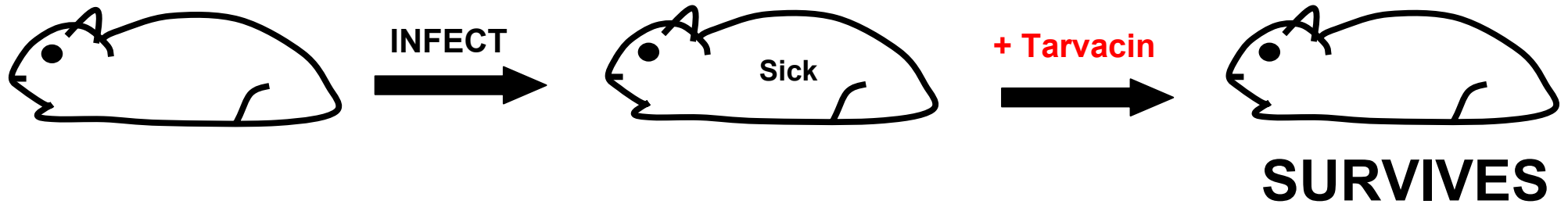


+ Pichinde virus

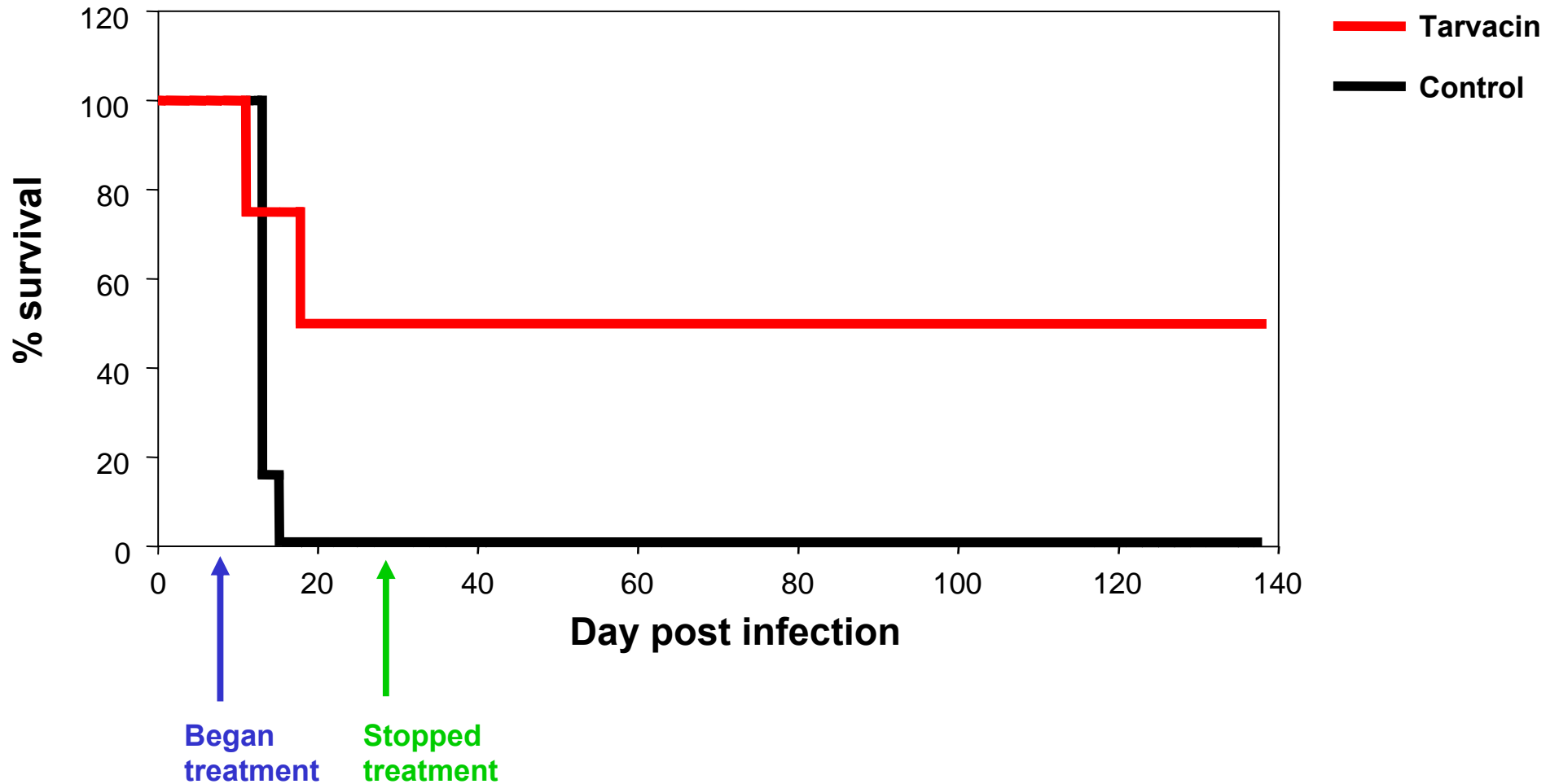


ANTI-PICHINDE VIRUS EFFECT OF TARVACIN IN VIVO

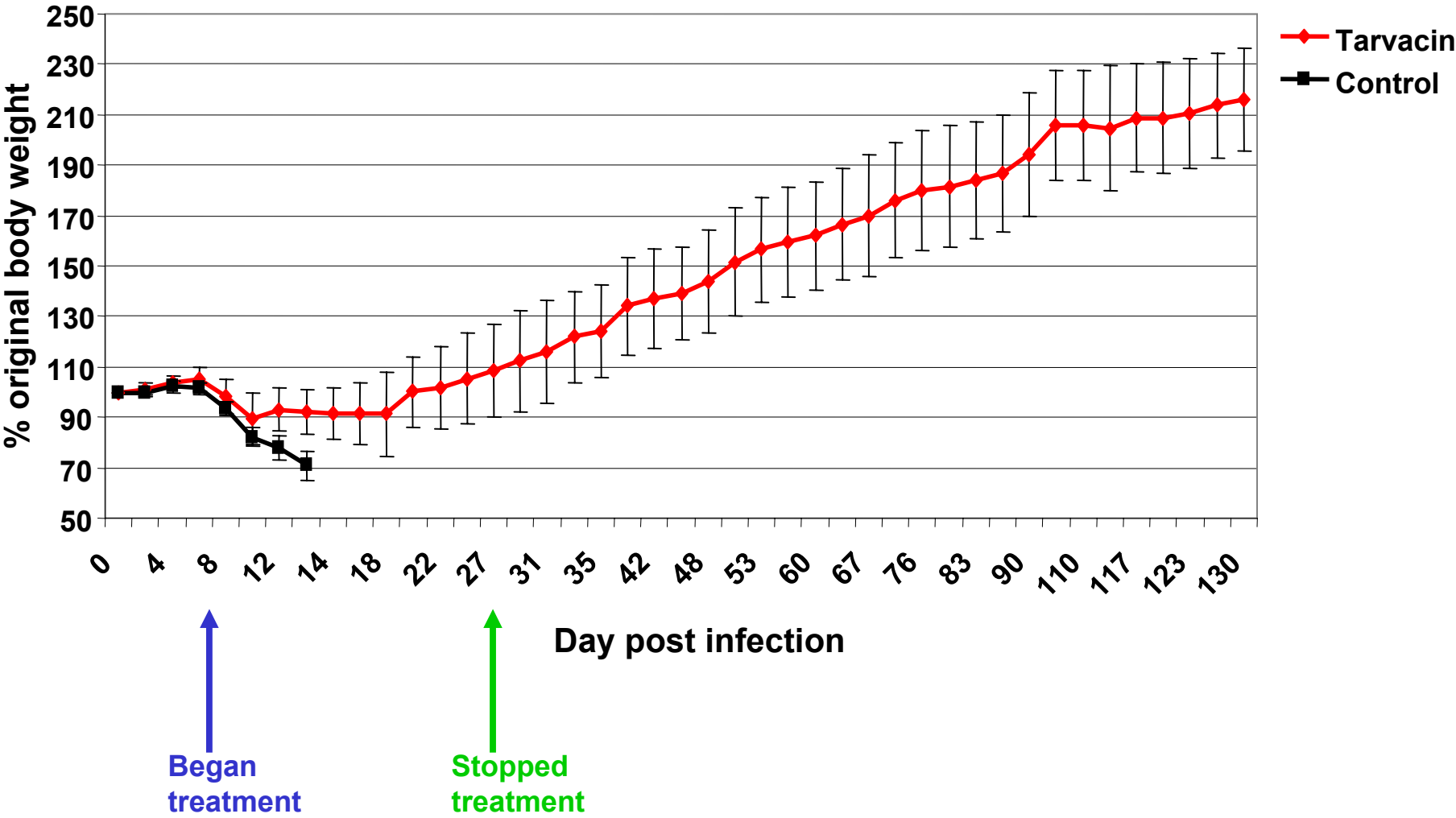
TREATMENT OF GUINEA PIGS INFECTED WITH PICHINDE VIRUS



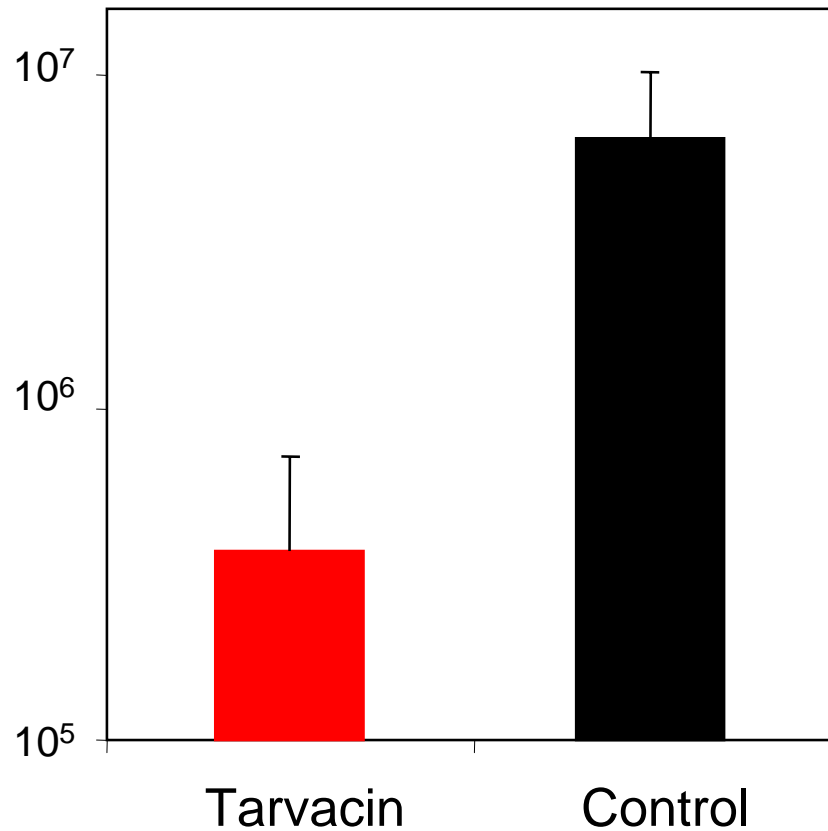
TREATMENT OF GUINEA PIGS WITH OVERT SYMPTOMS OF DISEASE ENHANCES SURVIVAL



TREATMENT OF GUINEA PIGS WITH OVERT DISEASE SYMPTOMS

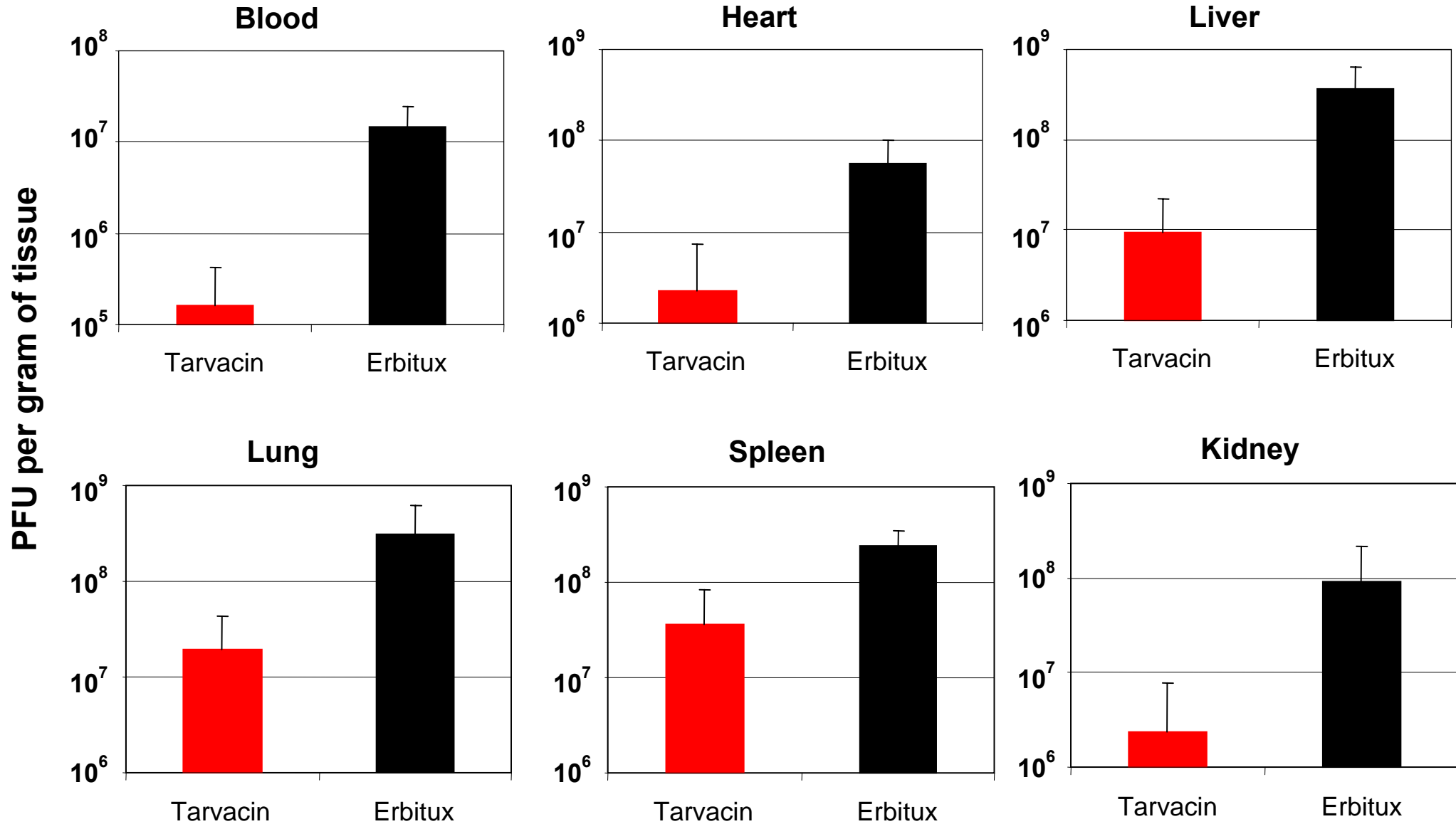


VIRAL LOAD IN THE BLOOD ONE DAY AFTER TREATMENT

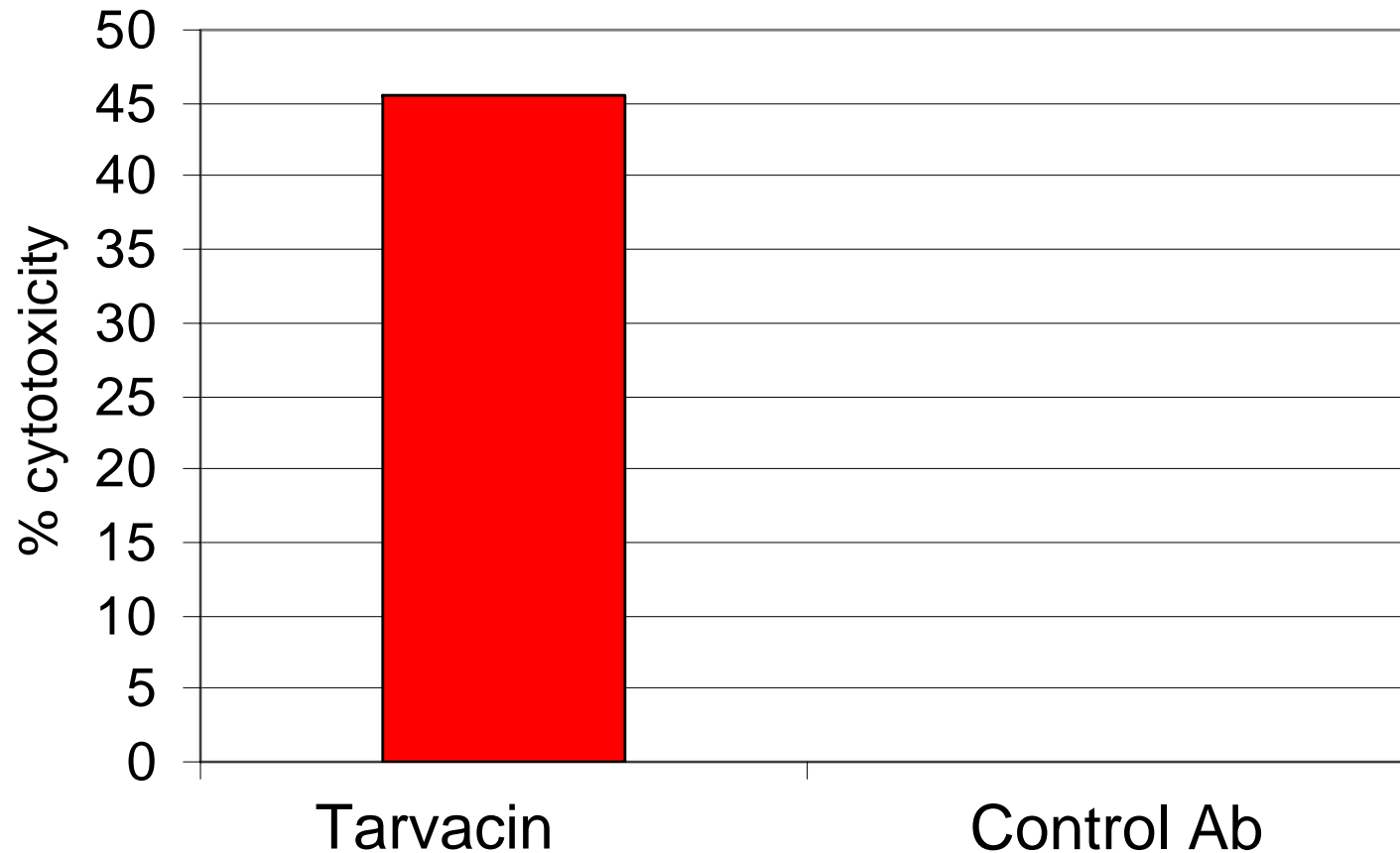


** No decrease is seen in any other tissues at this time point

TREATMENT OF GUINEA PIGS WITH OVERT DISEASE WITH TARVACIN REDUCES VIRAL LOAD IN MAJOR ORGANS AT DAY 14



TARVACIN MEDIATES ADCC OF INFECTED CELLS IN VITRO

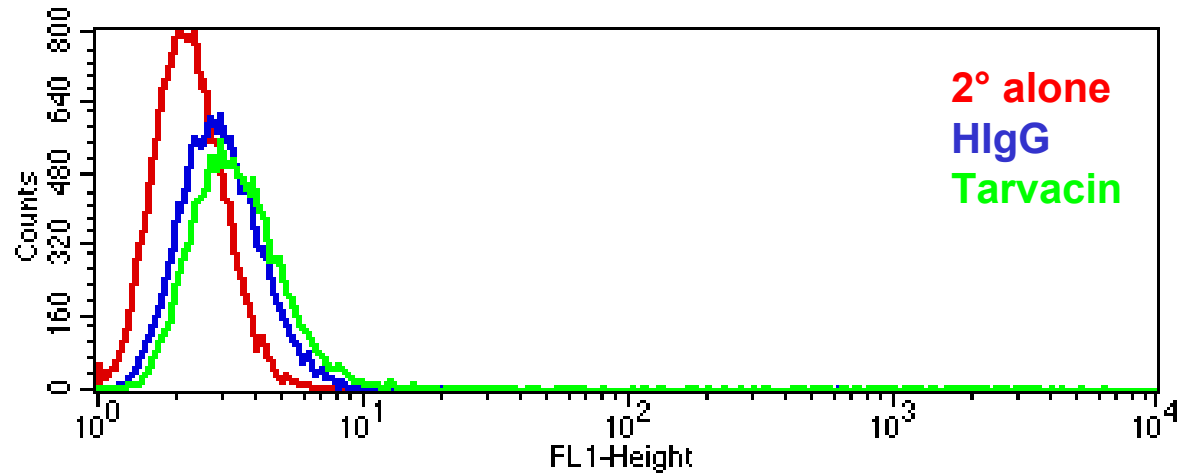


TARGETTING OTHER ENVELOPED VIRUSES

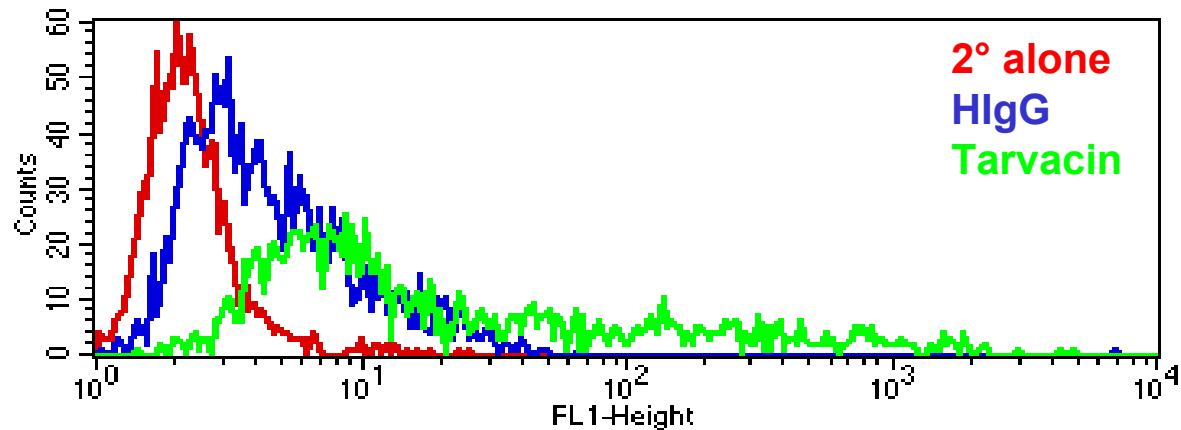
Tarvacin™ Binding				
Virus Family	Virus	Envelope	MODEL FOR	
<i>Arenaviridae</i>	Pichinde	Yes	+++	Lassa Fever
<i>Flaviviridae</i>	Bovine viral diarrhea	Yes	+++	Hepatitis C
<i>Herpesviridae</i>	Varicella-zoster virus 1	Yes	+++	Shingles
<i>Orthomyxoviridae</i>	Influenza A	Yes	+++	Flu
	Influenza B	Yes	+	Flu
<i>Paramyxoviridae</i>	Bovine parainfluenza 3	Yes	++	Flu
	Measles	Yes	+++	Measles
<i>Retroviridae</i>	Respiratory syncytial virus	Yes	+++	Pneumonia
	Feline immunodeficiency virus	Yes	++	AIDS
	Human immunodeficiency virus 1	Yes	+++	AIDS
	Human immunodeficiency virus 2	Yes	+++	AIDS
	Simian immunodeficiency virus	Yes	+++	AIDS
<i>Adenoviridae</i>	Adenovirus	No	?	Hepatitis
<i>Picornaviridae</i>	Coxsackie A	No	-	Enteric disease
	Coxsackie B	No	-	Enteric disease
	Echovirus	No	-	Febrile disease
	Enterovirus	No	?	Enteric disease
	Polio	No	?	Polio

BINDING OF TARVACIN TO VACCINIA VIRUS-INFECTED HUMAN MONOCYTC U937 CELLS

No virus

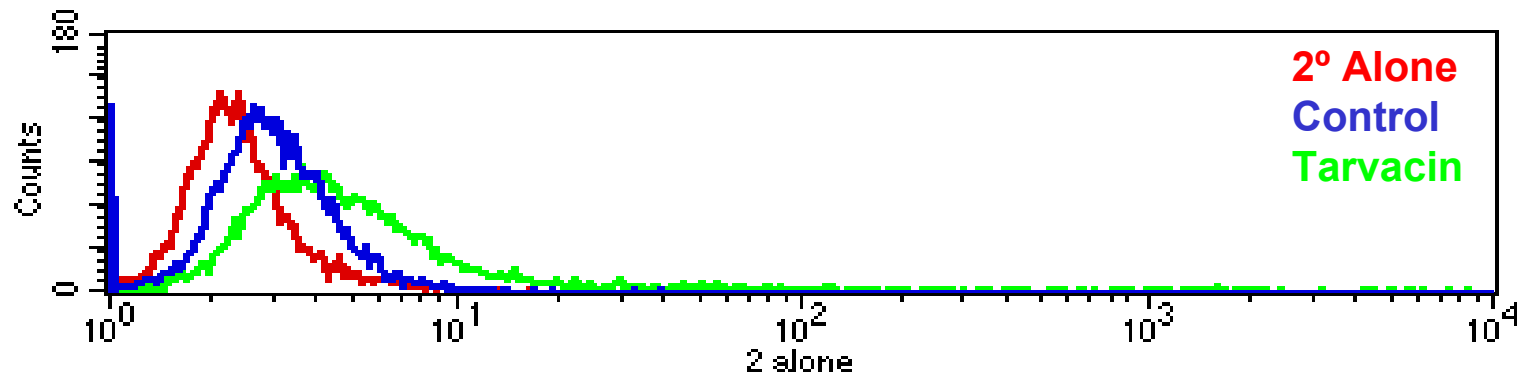


+ Vaccinia virus

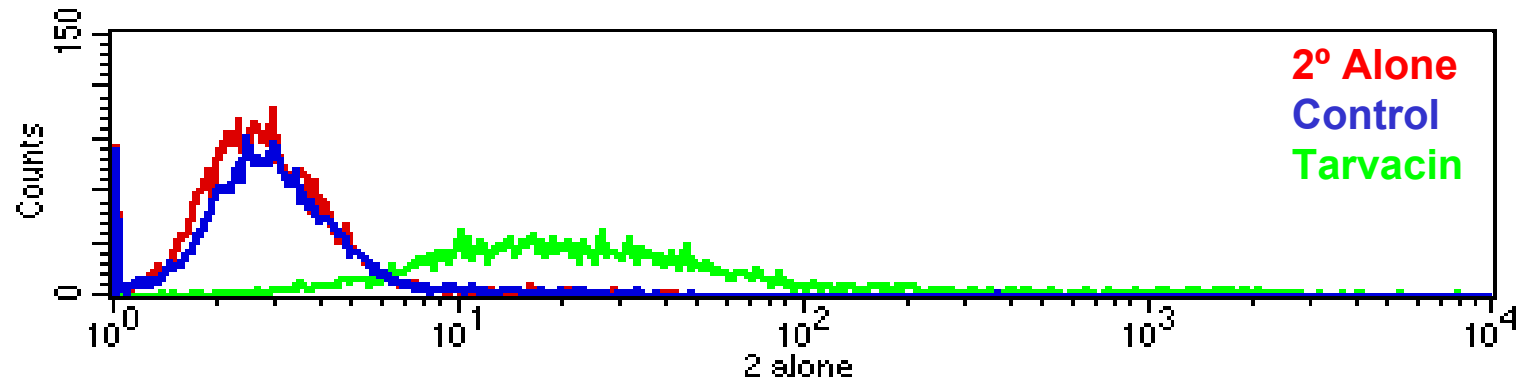


BINDING OF TARVACIN TO U937 CELLS INFECTED WITH INFLUENZA VIRUS

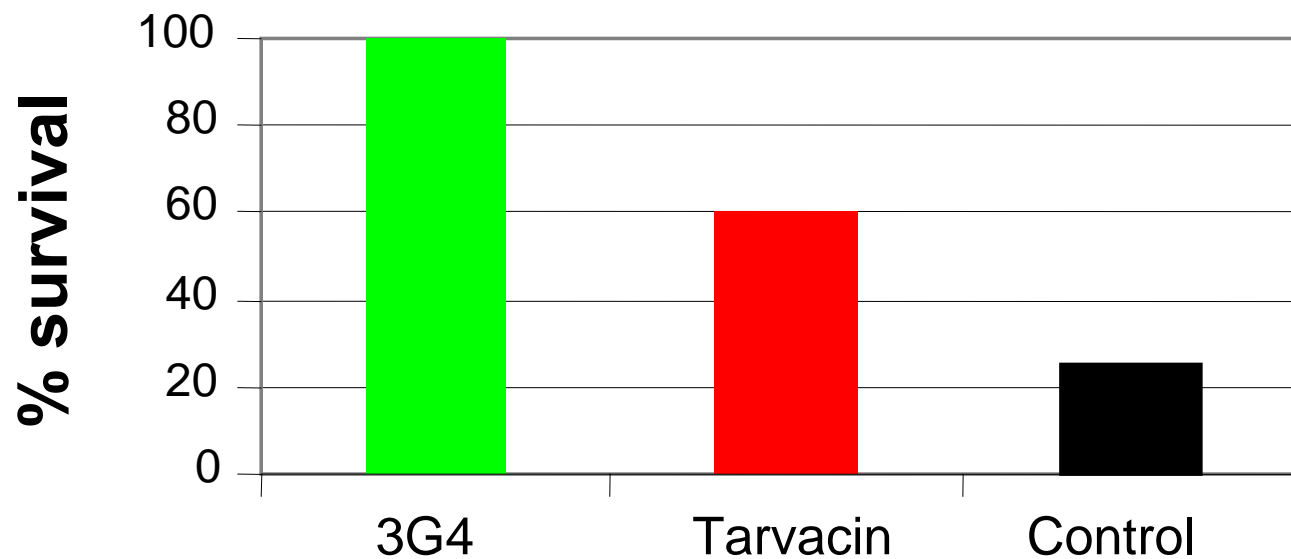
No Virus



+ Influenza



SURVIVAL IN BALB/c MICE INFECTED WITH mCMV



CLINICAL DEVELOPMENT OF TARVACIN

- PHASE 1 clinical trial has just been completed
- Patients: Chronic Hepatitis C patients who either no longer respond to or failed standard therapy with pegylated interferon and ribavirin combination therapy
- Center: Bach and Godofsky Infectious Diseases Center in Bradenton
- Results: Tarvacin was well tolerated with no serious adverse events reported in any of the 24 patients at any of the four dose levels tested

SUMMARY & CONCLUSIONS

Lassa Virus Model

- Tarvacin binds to Pichinde virus and to Pichinde-virus infected cells
- Treatment of lethally infected guinea pigs with Tarvacin results in 50% survival (reduced viral loads, no disease symptoms)-may be due to direct clearance of free virus and ADCC mechanisms
- Tarvacin-treated survivors completely clear virus and are resistant to reinfection

SUMMARY & CONCLUSIONS (continued)

Other Virus Models

- 3G4 treatment leads to 100% survival of Balb/c mice infected with an LD80 dose of mCMV virus
- 3G4 inhibits RSV and VSV in vitro (data not shown)
- Tarvacin binds to multiple enveloped viruses
- Tarvacin binds to Influenza-, Vaccinia- and HIV-infected cells

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Avid Bioservices

